Before Dr. Rowley, few scientists suspected that chromosomal aberrations caused cancer. Beginning in the 1970s, however, she made a series of fundamental discoveries demonstrating that specific chromosomal changes caused certain types of leukemia.

Changing the Paradigm

Dr. Rowley’s discoveries changed the way cancer was understood, opened the door to development of drugs directed at the cancer-specific genetic abnormalities, and created a model that still drives cancer research. “Janet Rowley’s work established that cancer is a genetic disease,” said Mary-Claire King, professor of genetics and medicine (medical genetics) at the University of Washington and president of the American Society of Human Genetics. “She demonstrated that mutations in critical genes lead to specific forms of leukemia and lymphoma, and that one can determine the forms of cancer present in a patient directly from the genetic changes in the cancer. We are still working from her paradigm.” Nevertheless, she struggled for years to convince fellow researchers. “I became a kind of missionary,” she often recalled, preaching that chromosome abnormalities were important and hematologists should pay attention to them. “I got sort of annoyed, tolerance at the beginning,” Dr. Rowley said. But thanks to her persistence and a long list of related discoveries, her idea gained credence. Eventually, they brought her widespread recognition, including the Lasker Award, the National Medal of Science, and the Presidential Medal of Freedom.

A Hero to Many

“Janet Rowley is a hero to many, including me,” said Brian J. Drucker, MD, director of the Oregon Health & Science University Knight Cancer Institute. “Her groundbreaking work on the identification of the reciprocal translocation between chromosome 9 and 22 in patients with chronic myelogenous leukemia allowed the development of the life-saving treatment Gleevec for this disease.”

Janet Rowley was a pioneer in what is now called translational research, the direct application of laboratory studies to understanding and treating human disease,” said Richard L. Schilsky, MD, a former colleague at the University of Chicago, and now chief medical officer of the American Society for Clinical Oncology. “She laid the foundation for personalized cancer care and targeted therapy.”

“She developed the Rosetta Stone that has enabled us to begin to dissect leukemias and lymphomas, to understand their progression and how they respond to treatment,” said blood cancer specialist Richard Larson, MD, professor of medicine at the University of Chicago. “Within my practice lifetime, her discoveries have led to the development of medicines that dramatically altered the management of fatal diseases like chronic myelogenous leukemia. We can now treat those patients on an outpatient basis with oral drugs that are well-tolerated and highly effective.”

A Lasting Impact

She also had an impact on the relationship between medical research and public policy. President Jimmy Carter appointed her to the National Cancer Advisory Board (1979-1984). President Bill Clinton awarded her the National Medal of Science (1998). From 2002 to 2009, she served on George W. Bush’s President’s Council on Bioethics. In 2009, she stood next to President Barack Obama when he lifted the federal moratorium on funding for stem cell research and she returned to the Obama White House later that year to accept the Presidential Medal of Freedom.

“Janet has been a mentor for her colleagues as well as her trainees and an ongoing example of scientific wisdom and imagination combined with impeccable personal and professional style,” said Michelle Le Beau, PhD and Arthur and Marian Edelstein Professor of Medicine and director of the University of Chicago Medicine Comprehensive Cancer Center. “She received just about every imaginable honor. Yet she remained breathtakingly humble, giving most of the credit to her colleagues, her students, and luck.”

Dr. Rowley died from complications of ovarian cancer on December 17, 2013, at her home. She was 88.
Catching up with Comer

Since opening its doors in 1967, the University of Chicago Medicine Comer Children’s Hospital has provided comprehensive, innovative medical care to children of all social and economic backgrounds. That mission will continue with the opening of the meta-sodiumyl-
gasimine (MIBG) room in 2014, the first of its kind in Chicago, for the treatment of nerve tissue tumors in infants and young children, called neuroblastoma. MIBG is a chemical that is selectively absorbed by neuroblastoma cells, which are then destroyed by the emitted radiation. Patients will stay in the lead-lined room for three to five days after receiving treatment to allow for recuperation and the radiation dose to wear off.

MIBG is the most effective treatment for children with relapsed neuroblas-
toma right at home.”

Comer recently became the recipient of a very big gift for very little people. The family behind the iconic Weber grill donated $10 million to support neonatal care at Comer. The pledge, made by the Stephen family of Weber-Stephen Products, was announced in September, at a neonatology reunion of former patients, their families, and the staff members who cared for them. In recogni-
tion of the Stephen’s support, the neonatology center was renamed the Margaret M. and George A Stephen Neonatal Intensive Care Unit (NICU). The gift, among the Chicago area’s largest, earmarked for neonatal care, will support research toward advancements in treatments for critically ill and prematu-
ture newborns, along with genetic studies to uncover links to early childhood diseases. The donation also enables the future recruitment of a Stephen Family Professor of Pediatrics. The Stephens NICU is the largest facility of its kind in the Midwest and admits about 1,000 babies annually.

A recent addition to Comer is an inter-
nationally recognized authority on pediatric surgical oncology. In August, Jessica Kandel, MD, was appointed as section chief of pediatric surgery, professor of surgery, and surgeon-in-chief of Comer. She has devel-
oped groundbreaking clinical treatments for vascular anomalies in children, while her research in angiogenesis has contributed to the development of an FDA-approved drug now widely used in the treatment of lung, breast, and certain brain and pediatric cancers.

Open Cancer Clinical Trials

Patient enrollment is under way for more than 350 clinical trials at the University of Chicago Medicine Comprehensive Cancer Center. A few of our newly launched clinical trials include:

• Selection of chemoradiotherapy based on response to induction chemotherapy, a Phase II study in locally advanced squamous cell carcinoma of the head and neck. Victoria Villafae, MD, principal investigator.
• A Phase II protocol for patients with stage 1/2 bladder cancer to evaluate selective bladder preserving treat-
ment by radiation therapy concurrent with cisplatin chemotherapy following a thorough transurethral surgical re-staging. Stanley Laiw, MD, principal investigator.
• Ablation in advanced refractory urothelial cancer: Peter O’Donnell, MD, principal investigator.
• Carboplatin, gemcitabine, and mitoxantrone for advanced breast cancer and recurrent or persistent epithelial ovarian cancer—Rita Nanda, MD, principal investigator.

To learn more about these or any other UCCCC clinical trial, call toll-free 1-855-702-8222 for adult clinical trials or 1-773-702-6180 for pediatric clinical trials, or go to cancer.uchicago.edu and click on Search Clinical Trials in the blue box.
Radiation Exposure: An Unchecked Risk

As early as before World War II, radiation was used for a cure-all for a multitude of diseases and benign ailments—from acne to tonsils and adenoids and enlarged thymus. However, there was little concern about the medical consequences of radiation exposure. The long-term medical effects that were recognized following the atom bomb blasts at Hiroshima and Nagasaki at the end of World War II raised public concern about the harmful consequences of radiation exposure, even low-level exposure. However, it was a study led by Dwight Clark, professor of surgery at the University of Chicago, in 1955 that showed 10 percent of these children later developed thyroid cancers. Additional papers from the University of Chicago showed the association between radiation exposure and thyroid cancer in adults, as well as in children. By the late 1960s, tighter controls on radiation use were implemented, but patients who had received low-dose radiation to their head or neck as children continued to be treated for thyroid cancer as adults. Edwin Kaplan, MD, professor of surgery, came to the University of Chicago Medical Center in 1971 and joined Drs. Leslie DeGroot and Samuel Refetoff to address this “Chicago Endemic.” Studies identified many patients who had received low-dose radiation to their neck as children and were found to have thyroid cancer as young adults. These reports led to consideration of public anxiety and attention. Large recall programs for at-risk patients were conducted across the Midwest. An analysis of 5,300 children who had received low-dose radiation to their head and neck at Michael Reese Hospital showed that 10 percent of these children later developed thyroid cancer.

As the research epicenter, the University of Chicago even hosted a National Institutes of Health-funded symposium on radiation-induced thyroid cancer in 1976. The University of Chicago research team continued to contribute significantly to this field well into the 1990s, including showing that radiation-induced thyroid cancer was not more aggressive than other thyroid cancers, as originally thought.

Rates on the Rise

Although the era of the “Chicago Endemic” has long passed, and while most other cancers have decreased in incidence, thyroid cancer rates have risen dramatically in the past few decades—6% to 8% per year, especially in young women. Recent work by Raymond Grogan, MD, assistant professor of surgery; Brian Chiu, PhD, associate professor of health studies; Xa-Chen Tiu Shuh, PhD, associate professor of medicine; and Dr. Kaplan, as well as Brijesh Aschhebrook-Kilfoy, PhD, research associate in health studies, projects that papillary thyroid cancer will double in incidence by 2019 and become the third most common cancer in women of all ages after breast and lung cancer. Unfortunately, the lack of funding and attention to thyroid cancer nationally means that research has lagged behind efforts made in most other cancers.

Current Research Efforts Under Way

Dr. Grogan and his research team, including Dr. Kaplan, Rex Weiss, MD, chief of endocrinology, and Shawn Kaplan, recently took a closer look at the University of Chicago cohort with an unprecedented median follow-up of 27 years. They found that lifetime recurrence rates for papillary thyroid cancer were 28%, and 11% of recurrences and 17% of deaths from papillary thyroid cancer occurred 20 years or more after the original diagnoses. These data inform how thyroid cancer survivors are monitored and support life-long surveillance of these patients.

Such research also highlights the need to elucidate the molecular basis of primary thyroid cancer, as well as causes of recurrence and metastasis, and how risk factors such as known environmental exposures are contributing to these rising thyroid cancer rates. Current research efforts include genetic studies by Dr. Grogan’s group in collaboration with Keesan Onel, MD, PhD, associate professor of pediatrics, and Hubbel Alham, MD, Louis Block Professor of Health Studies, to identify mutations in thyroid cancer specimens to uncover the molecular drivers of cancer and DNA variants that affect the risk of developing thyroid cancer after low-level radiation exposure. These research avenues create optimism that, despite the growing incidence and healthcare burden associated with thyroid cancer, advances in prevention, management, and treatment are emerging.

Dr. Kaplan and Grogan agree that “there is still a great deal of work to do.”

Thyroid Cancer: A Storied Past and Promising Future at the University of Chicago

The endocrine surgery team who treats cancers of the thyroid and other endocrine disorders at the University of Chicago Medicine includes Edwin Kaplan, MD, professor of surgery; Raymond Grogan, MD, associate professor of surgery; and Peter Angelos, MD, Linda Kohler Andersson Professor of Surgery. They have laid the foundation for the innovative approaches and groundbreaking science that are tackling the growing clinical challenges of thyroid cancer.

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Collaboration Drives Cancer Epigenome Mapping and Translation to the Clinic

Sometimes it takes a new discovery to put puzzling research findings into the right framework and bring their implications into sharper focus. This was the case for Lucy Godley, MD, PhD, associate professor of medicine, when the modified cytosine base known as 5-hydroxymethylcytosine (5-hmC) was described. Unprecedented data collected in her cancer epigenetics research laboratory finally made sense. The standard techniques that everyone had been using to identify these changes on DNA, such as bisulfit sequencing, could not distinguish between the well-characterized 5-methylcytosine (5-mC) and 5-hmC. These new insights also suggested that distinct epigenetic modifications might hold promise as a basis for new personalized medicine approaches for cancer patients.

Epigenetics is the study of heritable changes in gene activity that are not caused by alterations in DNA sequence but rather by modifications to DNA bases and histones. DNA methylation, typically at cytosine bases (i.e. 5-mC), is the best studied epigenetic mark that differs between normal and cancer cells. In many but not all cases, the genome of tumor cells contains significantly less global methylation compared to normal cells although specific tumor suppressor genes can be more highly methylated locally, leading to silencing of that gene. These modifications are thought to be so important to cancer cells that inhibition of the enzymes that catalyze the addition of the methyl group onto DNA, called DNA methyltransferases, have been approved for use in some blood cancers and are in clinical trials for others. However, the discovery of 5-hmC suggests that in the future, we may have a better understanding of the predictive power of 5-mC and/or 5-hmC genome signatures or profiles that predict response to these drugs.

A major advance in these efforts came when Chuan He, PhD, professor of chemistry and investigator of the Howard Hughes Medical Institute, and his colleagues developed the first chemical labeling approach to isolate 5-hmC-enriched DNA sequences. Using innovative chemistries, this strategy allowed for the construction of the first genome-wide maps of 5-hmC marks in a number of cell lines and tissue types in a collaborative project with Dr. Godley, and other colleagues. Further fine-tuning of the technical approaches has allowed for single-base resolution genome-wide sequencing of 5-hmC compared to 5-mC marks and reduction of the amount of starting material necessary for analysis. He’s group also demonstrated that TET proteins, which are required for 5-hmC formation, can catalyze additional cytosine modifications, including 5-formylcytosine (5-fC) and 5-carboxycytosine (5-cfC). Currently, he is training up with other cancer researchers at the University of Chicago and world-wide to assess changes in the epigenome among various tumor types, including breast and colorectal cancer, with his eye toward developing new diagnostic and prognostic tools.

“By achieving these technological breakthroughs, we are able to define the epigenetic signature of cancers with only 1,000 cells. This was unthinkable just a year ago,” said Dr. He. He predicts that these tools may be used routinely in the clinical setting in less than five years, provided there are enough resources and samples available to validate the diagnostic and prognostic value of these signatures.

As an oncologist who treats patients with blood cancers, including leukemias and lymphomas, Dr. Godley is also interested in translating her research into the clinic. Her team has recently discovered, in collaboration with Amanda Wickrema, PhD, associate professor of medicine, and Dr. He, that 5-hmC levels are dynamically controlled during the differentiation of human red blood cells. The function of these marks appears to control transcription factor binding and subsequent gene expression during differentiation, such that dysregulation of the epigenome in hematopoietic cells is associated with a block in red blood cell differentiation (a hallmark of this cancer).

In a separate study, the Godley group has collaborated with M. Eileen Dolan, PhD, professor of medicine, and Wei Zhang, PhD (University of Illinois at Chicago), to examine how covalent cytosine modifications influence the phenotype of gliomas, an aggressive type of brain tumor. By targeting these modifications, including the addition of the methyl group onto DNA, called DNA methylation, typically at cytosine bases (i.e. 5-mC), is the best studied epigenetic mark that differs between normal and cancer cells. In many but not all cases, the genome of tumor cells contains significantly less global methylation compared to normal cells although specific tumor suppressor genes can be more highly methylated locally, leading to silencing of that gene. These modifications are thought to be so important to cancer cells that inhibition of the enzymes that catalyze the addition of the methyl group onto DNA, called DNA methyltransferases, have been approved for use in some blood cancers and are in clinical trials for others. However, the discovery of 5-hmC suggests that in the future, we may have a better understanding of the predictive power of 5-mC and/or 5-hmC genome signatures or profiles that predict response to these drugs.

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1 Kevin Roggin, MD, associate professor of surgery, has been elected to a three-year term on the Society of Surgical Oncology (SSO) Executive Council. Associate Professor of Surgery 2 Swati Kulkarni, MD, was awarded the 2013-2015 Clinical Investigator Award in Breast Cancer Research from the SSO’s James Ewing Foundation. She will use the two-year grant for her project, “Bariatric surgery alters cholesterol availability and estrogen receptor alpha activity in postmenopausal women.”

3 David W. Chang, MD, FACS, a leading authority on surgical treatment of lymphedema—a severe build-up of fluid caused by cancer and cancer treatment—has been appointed professor of surgery at the University of Chicago Medicine. Dr. Chang has been a key player in introducing lymphaticovenular bypass, a novel treatment for lymphedema. He is one of a few surgeons in the country, and the only one in Illinois, who performs it routinely. Dr. Chang comes to the University of Chicago Medicine from the University of Texas MD Anderson Cancer Center in Houston, where he was a professor of plastic surgery, deputy chair of the department, and director of the plastic surgery clinic and the center for microsurgery research and education.

4 Asim Padela, MD, MSc, assistant professor of medicine, was invited to present research updates at a benefit dinner for the Initiative on Islam and Medicine November 23 in Oak Brook. Dr. Padela is the director of the University of Chicago Initiative on Islam and Medicine. His research explores ways in which religious beliefs, values, and identity impact the health-related behaviors of both American Muslim patients and healthcare providers.

5 David Rubin, MD, professor of medicine, has been named interim section chief of gastroenterology, hepatology and nutrition at the University of Chicago Medicine. Dr. Rubin currently serves as co-director of the medical center’s Inflammatory Bowel Disease Center. He studies novel therapies for Crohn’s disease and ulcerative colitis, colon cancer prevention, and clinical medical ethics. He is the principal investigator for multiple clinical research projects and trials of novel therapies, including the first Food and Drug Administration-authorized study of fecal microbiota transplantation for ulcerative colitis.

6 David Song, MD, MBA, Cynthia Chow Professor of Surgery and chief of plastic and reconstructive surgery, was named by the University of Chicago Medicine as the first Associate Dean for Continuing Medical Education (CME). In this role, Dr. Song will work closely with a strategic planning committee to identify the goals and strategies for CME programming and to develop initiatives to align with the changing focus of professional development.

The Leukemia Research Foundation selected Katherine Breitenbach, RN, MSN, APN, NP-C, for the 2013 Nurse of the Year Award. Ms. Breitenbach is a nurse practitioner in the Leukemia and Bone Marrow Transplant Program at the University of Chicago Medicine. She was nominated by two of her colleagues, Carol White, RN, MSN, AOCN, who won the award in 1997, and Wendy Stock, MD, professor of medicine and director of the leukemia program. She received a plaque, as well as a monetary award for herself and her unit.

The following talks were given by UCCCC members Andrew Artz, MD: Oral session, “Allogeneic transplant for high-risk myelodysplastic syndromes and acute myeloid leukemia,” and Education program, “Older patients/older donors: Choosing wisely,” Christopher Daugherty, MD: Education spotlight, “Defining the transition point and the challenges of prognosis disclosure” Lucy Godley, MD: Special interest session, “Leukemia/stem cell transplant” Olatoyosi Oderinle, MD: Education program, “Bendamustine in the management of myelofibrosis” Sonali Smith, MD: Education program, “Dissecting follicular lymphomas: high versus low risk” Wendy Stock, MD: Session moderator, Late-breaking Abstracts Sessions Members whose work was also presented as poster and/or paper presentations include: Dr. Artz, Dr. Daugherty, Dr. Godley, Dr. Oderinle, Dr. Smith, Dr. Stock; Jiansun Chen, PhD; Brian Chiu, PhD; Jill de Jong, MD, PhD; Sandeep Gurbuxani, PhD; Andrei Jakubowski, MD, PhD; Justin Klein, MD, PhD; Richard Larson, MD, Michelle Le Beau, PhD; director of the University of Chicago Medicine Comprehensive Cancer Center; Yuuka Nakamura, MD, PhD; Kenan Onel, MD, PhD, and Annyria Wickrema, PhD.

San Antonio Breast Cancer Symposium December 14-18, 2013 San Antonio, TX For more than three decades, San Antonio has been the site for bringing the worldwide breast cancer community together and highlighting its state-of-the-art advances in basic, clinical, and translational breast cancer research. The following UCCCC members presented their work: M. Eileen Dolan, PhD; Dezheng Huo, MD, PhD; Swati Kulkarni, MD; Rita Nanda, MD; and Olufunmilayo Olopade, MD. Breast cancer survivor and University of Chicago Breast A.KEEPE SPORTE advocate, Shirley Mertz, also presented at the conference. American Society for Cell Biology (ASCB) Annual Meeting December 14-18, 2013 New Orleans, LA ASCB represents an international community of cell biologists, and its annual meeting is dedicated to showcasing research in basic biology at the level of the cell, including cancer cells, and promoting scientific exchange among its members.

Benjamin Gluck, PhD, a member of the ASCB Council, participated in the Science Discussion Roundtables and had his research presented in several posters.

Tara Henderson, MD, MPH: General session, “Opportunities and challenges in managing comorbidities among disadvantaged populations” Karen E. Kim, MD, MS: Hot topics session, “Patient-provider communication and colorectal cancer screening in three Asian communities” In addition, eight research posters were presented by the University of Chicago Medicine Comprehensive Cancer Center Office of Community Engagement and Cancer Disparities. Under the direction of Dr. Kim, 55th American Society for Hematology (ASH) Annual Meeting and Exposition December 7-10, 2013 New Orleans, LA As the largest professional organization dedicated to understanding and treating blood disorders, including cancer, the ASH annual meeting is the premier platform where leaders in hematopoietic malignancy clinical care and research converge to exchange ideas and research advancements.
Milky Spots and Adipose in the Omentum Promote Metastasis of Ovarian Cancer Cells

The increased presence of ovarian cancer cells to escape from the primary tumor and form metastases in the abdominal cavity is a major clinical challenge and significant cause of morbidity and mortality in ovarian cancer patients. The omentum, a fold of peritoneum composed of immune and stromal cell-rich milky spots and adipose that cover and support abdominal structures, is a common site of ovarian cancer metastasis. Carrie Rinker-Schaeffer, PhD, professor of surgery, and her team hypothesized that the omentum microenvironment plays an active role in facilitating ovarian cancer metastatic colonization.

Using in vivo models, they demonstrated that human ovarian cancer cells preferred to grow in omental adipocyte milky spots rather than peritoneal fat, and there was an inverse relationship between ovarian cancer cell growth and adipocyte area in the same omentum. The effort to understand the mechanism responsible for omentum-dependent metastasis, they employed a novel ex vivo mouse model and discovered that mitochondrial gene expression and the presence of a factor(s) that promotes ovarian cancer cell migration. This work highlights the complex interplay between ovarian cancer cell migration and mitochondrial microenvironment and serves as a foundation for developing innovative strategies to interfere with ovarian cancer metastasis into the peritoneum. (Clark et al., Am J Obstet Gynecol 183:576-91, 2011)

CHROMATIN INTERACTIONS CONTROL GENE REGULATION AND CELL FATE

Straddling the fields of signal transduction, translational biology, and cancer biology, Ilaria Rebay, PhD, professor of the Ben May Department for Cancer Research, focuses her research efforts on understanding the molecular mechanisms of gene regulation that control cell proliferation, fate specification, differentiation, and survival. Her group recently investigated how various signaling pathways and cell-cell interactions prevent inappropriate cell fate specification. They demonstrated that an exhaustive search algorithm could distill an existing 950-gene expression signature down to two or three features with equal discrimination. Validation of the two-gene signatures was accomplished using three additional independent datasets. By further extending the work to a lung cancer dataset, the investigators showed that this strategy could be generalized and applied to other cancer types. The team identified signatures that are only modestly correlated. Routine clinical use. Importantly, their methodology is being developed as open source software for the cancer research community to enhance the impact and clinical relevance of the work. (Wilson et al., Cancer Res 73:5625-32, 2013)

EMERGENCE OF RAS/RAF/MEK/ERK SIGNAL TRANSDUCTION PATHWAYS AS A CLINICAL ENDPOINT AND BIOMARKER

In phase I MEK Inhibitor Clinical Trial Confirms Safety and Anti-Leukemic Activity

The RAS/RAF/MEK/ERK signal transduction pathway is aberrantly activated in 70-80% of acute myeloid leukemias (AML), and inhibition of MEK in preclinical studies has shown promising anti-tumor effects. However, the clinical relevance of these findings was poorly understood. Olatoyo Odienneke, MBBS, associate professor of medicine, and colleagues including Wendy Stock, MD, professor of medicine, Richard Larson, MD, professor of medicine; Walter Stadler, MD, Fred C. Buzdar, PhD, professor of medicine; and Theodore Kerrison, PhD, research associate (professor of health) conducted the phase II multi-center study. The single-agent silmitasertib, a potent and selective orally bioavailable small molecule MEK1/2 inhibitor, in patients with advanced AML. They found that the drug had a favorable toxicity profile and was associated with modest anti-leukemic activity (i.e. 6/16 patients had a response). A single nucleotide polymorphism (SNP) in the RAS gene, that may distinguish patients not benefiting from silmitasertib, was associated with poor clinical outcome. These results suggest that larger clinical trials with this agent are warranted and, given its safety profile, indicate that selumetinib may be particularly useful in combination with drugs that target other signaling pathways activated in AML, such as the PD1/AKT pathway. (Jain et al., Clin Cancer Res Epub ahead of print, 2013)

Pancreatic Cystic Neoplasms

USING IN VIVO MODELS, THEY DISCOVERED THAT THERE IS A CRITICAL MECHANISM FOR MALIGNANT TRANSFORMATION

Pancreatic cystic neoplasms include intraductal papillary mucinous neoplasms or mucus cystadenomas, which are premalignant lesions that require surveillance or consideration for surgery, yet they are often indistinguishable from benign pseudocysts and serous cysts. Development of a novel needle-based confocal laser endomicroscopy (nCLE) miniprobe may provide a means to detect these pancreatic cystic neoplasms. A team of UCCCC investigators including Yan Konda, MD, assistant professor of medicine, Irving Waxman, MD, professor of medicine, John Hart, MD, professor of pathology, and collaborators from other institutions assessed 66 patients from eight referral centers for the presence of epithelial villous structures using nCLE was associated with pancreatic cystic neoplasms at a high level of specificity and positive predictive value. However, a relatively low level of sensitivity suggests that this methodology may have limited application. Moreover, the associated overall complication rate of 9% indicates that safety of the approach also requires further study. (Konda et al., Endoscopy 45:1006-13, 2013)

mRNA STABILITY IS CONTROLLED BY N-METHYLDENOSINE

Many cancer-related genes, including oncogenes, tumor suppressors, tumor-promoting genes, and growth factors, are regulated post-transcriptionally, and, more specifically, at the level of mRNA turnover. Chuan He, PhD, professor of radiation and cellular oncology, and his research team uncovered a critical mechanism for dictating mRNA stability. In all higher eukaryotes, N-methyldenosine (m’A) is the most common internal (non-capping) mRNA modification. He’s group found that m’A is selectively recognized by a “reader” protein called YTH domain family 2 (YTHDF2) to regulate mRNA degradation. This is a translational approach, more than 3,000 cellular RNAs were identified as targets of YTHDF2. Further, the precise biochemical role of YTHDF2 in RNAs with the m’A modification was demonstrated that reversible m’A modifications may fine-tune mRNAs turnover via “readers” to modulate protein expression. (Wang et al., Nature 505:117-20, 2014)

Bell of Hope’s Signals the End of Patients’ Treatment

After being diagnosed with colon cancer and undergoing 10 radiation treatments at the University of Chicago Medicine Comprehensive Cancer Center at Silver Cross Hospital, Arthur Grindler and his daughters Barbara Widelski—a three time cancer survivor—and Laura Grindler wanted to express their gratitude to his physician Daniel Golden, MD, assistant professor of radiation and cellular oncology, and the entire care team that supported him. Arthur and Barbara donated an inspirational plaque and a shiny, gold bell to a shelf in hope and inspire cancer patients. After a final course of radiation treatment, they are encouraged to ring the ship’s bell three times in celebration. The plaque is adorned with an eagle in flight representing the courage and strength of the patients, and includes an inscription “Ring this bell... Three times well, its toll to clearly say, My treatment’s done, This course is run, And I am on my way!”
Experts at UChicago Medicine Treat Man with Inherited Condition That Led to Rare, Deadly Cancer

Many discoveries have been made by scientists looking through a microscope, beginning with early users Galileo Galilei, Robert Hooke, and Anton van Leeuwenhoek in the 17th century. Researchers still use microscopes to study how cells behave, but both the power of magnification and resolution of modern-day microscopes have increased to unprecedented levels. Now, microscopy increases our capability of seeing detail by 10,000 times so that objects as small as nanometers can be visualized. According to Vyta Bondokas, PhD, technical director of the Integrated Microscopy Core Facility, the field continues to advance, with new types of microscopy tools pushing the limit in innovation. “Modern optics have surpassed the diffraction limit, which means we are now seeing objects smaller than anyone had previously thought possible with the human eye.”

To help scientists at the University of Chicago Medicine Comprehensive Cancer Center stay abreast of these advances, the Integrated Microscopy Core Facility provides a wide range of instrumentation and image-analysis tools that allow for the most advanced imaging capabilities currently available. Because this type of technology is expensive for individual laboratories to obtain on their own, and relies on expertise that takes many years to develop, the Facility and its talented staff are a rich resource for Cancer Center investigators with instrumentation located in the Knapp Center for Biomedical Discovery and Abbott Memorial Hall, the Facility is accessible to users 24/7, with support staff available during normal business hours.

Within the past year, the Facility has announced the addition of two new systems. In late summer, they acquired a single-plane illumination microscopy system, the Zeiss LightSheet Z.1, in partnership with the Institute for Genomics & Systems Biology. This microscope utilizes a sheet of light through which the specimens move, producing a thin optical slice that is 2-10 microns thick. Christine Labno, PhD, co-technical director, said the camera-based system uses low-intensity laser light, which is gentle on the specimens. It is well-suited to capture time-lapse imaging of larger organisms, such as zebrafish, Drosophila (fruit fly) embryos, C. elegans (a type of worm), and small plants. The system can capture cyan, green, and/or red signals at very high detail and very high speed. The technology has also been used to image living and fixed 3-D cell cultures, including organisms, cysts, and 3-D cell migration assays to study cell migration and development.

The other instrument, which was purchased in November by the Institute for Genomics & Systems Biology, is the Leica Super-resolution 3-D Ground State Depletion system. This wide-field fluorescence microscope captures the images of individual molecules in two to three colors. In just a couple of minutes, the image is formed from these colored dots, similar to the “pointillist” technique. In addition, this microscope achieves lateral resolution down to 20 nanometers and vertical spatial resolution to 50 nanometers, which is nearly ten times better than confocal microscopy. Therefore, the system helps researchers visualize the 3-D location of molecules and structures at a level never possible before to better understand cellular processes. The system can localize three colors of localiza-

The Zeiss Lightsheet Z.1 is a microscope that utilizes a sheet of light through which specimens move, producing a thin optical slice that is 2-10 microns thick.
Grand Auction Raises More Than $1 Million for Cancer Research

The Women’s Board of the University of Chicago Cancer Research Foundation hosted the 47th Annual Grand Auction at the Four Seasons Hotel in November. Attendees celebrated this year’s theme, “Visionnaire,” with cocktails, dinner, dancing, a live and silent auction, and a tribute to Janet Rowley, MD, DSc, Blum-Riese Distinguished Service Professor of Medicine, Molecular Genetics and Cell Biology, and Human Genetics. The Women’s Board named Dr. Rowley this year’s recipient of the Partners in Discovery Award for her groundbreaking work in making the connection between cancer and genetics.

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